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CLAIMS:

1. A 38-residue CRFR1 ligand peptide which binds to CRFR1 with an affinity substantially greater than it binds to CRFR2, which peptide has the following formula, or a nontoxic salt thereof:

Y_1-Pro-Pro-R_6-Ser-R_8-Asp-R_{10}-R_{11}-D-Phe-R_{13}-R_{14}-R_{15}-Arg-R_{17}-R_{18}-R_{19}-R_{20}-R_{21}-R_{22}-R_{23}-R_{24}-R_{25}-R_{26}-R_{27}-R_{28}-R_{29}-Gln-Glu-R_{32}-R_{33}-R_{34}-Arg-R_{36}-R_{37}-R_{38}-R_{39}-R_{40}-R_{41}-NH_2 wherein Y_1 is an acyl group having not more than 15 carbon atoms or is radioiodinated tyrosine; R_6 is Ile, Met or Nle; R_8 is Leu or Ile; R_{10} is Leu or CML; R_{11} is Thr or Ser; R_{13} is His, Tyr or Glu; R_{14} is CML or Leu; R_{15} is CML or Leu; R_{17} is Glu, CML, Asn or Lys; R_{18} is Val, CML, Nle or Met; R_{19} is CML, Leu or Ile; R_{20} is Glu, D-Glu or His; R_{21} is Nle, Leu, CML or Met; R_{22} is Ala, D-Ala, Aib, Thr, Asp or Glu; R_{23} is Arg or Lys; R_{24} is Ala, Gln, Ile, Asn, CML or Aib; R_{25} is Asp or Glu; R_{26} is Gln, Asn or Lys; R_{27} is CML, Glu, Gln or Leu; R_{28} is Ala, Lys, Arg or Aib; R_{29} is Gln, Aib or Glu; R_{32} is Aib or an L- or D-isomer of a natural α-amino acid other than Cys; R_{33} is Aib or an L- or D-isomer of Ser, Asn, Leu, Ala, CML or Ile; R_{34} is Lys or Orn; R_{36} is Lys, Orn, Arg, Har, CML or Leu; R_{37} is CML, Leu, Nle or Tyr; R_{38} is Nle, Met, CML or Leu; R_{39} is Glu, Aib or Asp; R_{40} is Ile, Aib, CML, Thr, Glu, Ala, Val, Leu, Nle, Phe, Nva, Gly or Gln; and R_{41} is Ala, Aib, Ile, CML, Gly, Val, Leu, Nle, Phe, Nva or Gln; provided that a cyclizing bond may exist between Glu in position 31 and R_{34} and provided further that D-2Nal or D-Leu may be substituted for D-Phe.

abbreviations ? chief

2. A peptide according to claim 1 having the formula:

(cyclo 31-34)Y_1-Pro-Pro-R_6-Ser-R_8-Asp-Leu-R_{11}-D-Phe-His-R_{14}-Leu-Arg-Glu-R_{18}-Leu-R_{20}-Nle-R_{22}-R_{23}-Ala-R_{25}-Gln-Leu-Ala-R_{29}-Gln-Glu-R_{32}-R_{33}-R_{34}-Arg-R_{36}-R_{37}-Nle-R_{39}-R_{40}-R_{41}-NH_2 wherein Y_1 is an acyl group having not more than 7 carbon atoms; R_{20} is Glu or D-Glu; R_{22} is Ala or Thr; R_{29} is Gln or Glu; R_{32} is His, Aib, Ala, Gly, Leu, Gln or Glu; R_{36} is Lys or Leu; R_{37} is Leu or CML; R_{39} is Glu or Asp; R_{40} is Ile, CML or Glu; and R_{41} is Ile, Aib or Ala; with the remaining variables being as defined in claim 2.

3. A peptide according to claim 1 having the formula:

(cyclo 31-34)Ac-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val-Leu-Glu-Nle-Ala-Arg-Ala-Glu-Gln-Leu-Ala-Gln-Gln-Glu-His-Ser-Lys-Arg-Lys-Leu-Nle-Glu-Ile-Ile-NH_2, or

(cyclo 31-34)Ac-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val-Leu-Glu-Nle-Ala-Arg-Ala-Glu-Gln-CML-Ala-Gln-Gln-Glu-His-Ser-Lys-Arg-Lys-Leu-Nle-Glu-Ile-CML-NH_2; or
(cyclo 31-34)Ac-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val-Leu-Glu-Nle-Ala-Arg-Ala-Glu-Gln-CML-Ala-Gln-Gln-Glu-His-Aib-Lys-Arg-Lys-Leu-Nle-Glu-Ile-CML-NH_2.

4. A peptide according to claim 1 having the formula:
(cyclo 31-34)Ac-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val-Leu-Glu-Nle-Ala-Arg-Ala-Glu-Gln-Leu-Ala-Gln-Gln-Glu-His-Ser-Lys-Arg-Lys-Leu-Nle-Glu-Ile-Ile-NH_2, or
(cyclo 31-34)Ac-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val-Leu-Glu-Nle-Ala-Arg-Ala-Glu-Gln-CML-Ala-Gln-Gln-Glu-His-Ser-Lys-Arg-Lys-Leu-Nle-Glu-Ile-CML-NH_2; or
(cyclo 31-34)Ac-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val-Leu-Glu-Nle-Ala-Arg-Ala-Glu-Gln-CML-Ala-Gln-Gln-Glu-His-Aib-Lys-Arg-Lys-Leu-Nle-Glu-Ile-CML-NH_2.

duplicate

5. A CRF according to claim 1 having the formula:
Y_1-Pro-Pro-R_6-Ser-R_8-Asp-Leu-R_{11}-D-Phe-His-R_{14}-Leu-Arg-Glu-R_{18}-Leu-R_{20}-Nle-R_{22}-R_{23}-Ala-R_{25}-Gln-Leu-Ala-R_{29}-Gln-Glu-R_{32}-R_{33}-R_{34}-Arg-R_{36}-R_{37}-Nle-R_{39}-R_{40}-R_{41}-NH_2 wherein Y_1 is an acyl group having not more than 7 carbon atoms; R_{20} is Glu or D-Glu; R_{22} is Ala or Thr; R_{23} is Arg or Lys; R_{29} is Gln or Glu; R_{32} is His, D-His, Aib or Ala; R_{36} is Lys or Leu; R_{37} is Leu or CML; R_{39} is Glu or Asp; R_{40} is Ile, CML or Glu; and R_{41} is Ile, Aib or Ala; wherein the remaining variables are as defined in claim 2 and wherein the side chains of Glu^{31} and R_{34} may be covalently connected.

$R_{31} = Glu$

6. A peptide according to claim 1 wherein R_{18} is Val, R_{22} is Ala, R_{23} is Arg, R_{24} is Ala, R_{25} is Glu, R_{28} is Ala, R_{39} is Glu, and R_{41} is Ile.

7. A peptide according to claim 1 having the following formula, or a nontoxic salt thereof:
(cyclo 31-34)Y_1-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val-Leu-Glu-Nle-R_{22}-R_{23}-Ala-Glu-Gln-R_{27}-Ala-Gln-Gln-Glu-R_{32}-R_{33}-Lys-Arg-Lys-Leu-

Nle-Glu-R_{40}-Ile-NH_2 wherein R_{22} is Ala or Thr; R_{27} is Leu or CML; R_{32} is His or Aib; R_{33} is Ser or Aib; and R_{40} is Ile or CML.

8. A peptide according to claim 1 having the formula:
(cyclo 31-34)Ac-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val-Leu-Glu-Nle-Ala-Arg-Ala-Glu-Gln-Leu-Ala-Gln-Gln-Glu-His-Ser-Lys-Arg-Lys-Leu-Nle-Glu-Ile-Ile-NH_2, or
(cyclo 31-34)Ac-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val-Leu-Glu-Nle-Ala-Arg-Ala-Glu-Gln-CML-Ala-Gln-Gln-Glu-His-Ser-Lys-Arg-Lys-Leu-Nle-Glu-Ile-CML-NH_2; or
(cyclo 31-34)Ac-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val-Leu-Glu-Nle-Ala-Arg-Ala-Glu-Gln-CML-Ala-Gln-Gln-Glu-His-Aib-Lys-Arg-Lys-Leu-Nle-Glu-Ile-CML-NH_2.

3, 4, 8. duplicate

9. A peptide according to claim 1 which is useful as a tracer that selectively bonds to CRFR1 wherein Y is radioiodinated D-Tyr or L-Tyr. lack of antecedent.

10. A 38-residue CRFR1 ligand peptide which binds to CRFR1 with an affinity substantially greater than it binds to CRFR2, which peptide has the formula Y_1-Pro-Pro-A-D-Xaa-B-Glu-Xaa_a-Xaa_b-Xaa_c-C-NH_2 wherein Y_1 is an acyl group having not more than 15 carbon atoms or is radioiodinated tyrosine; A is a sequence of 6 amino acid residues that is found between Pro in the 5-position and Phe in the 12-position of r/hCRF or the corresponding sequence of another peptide of the CRF family; D-Xaa is D-Phe, D-2Nal or D-Leu; B is a sequence of 18 amino acid residues that is found between Phe in the 12-position and Ala in position-31 of r/hCRF or the corresponding sequence of another peptide of the CRF family; Xaa_a is any L- or D-natural α-amino acid other than Cys or is Aib; Xaa_b is Aib or an L- or D-isomer of Ser, Asn, Leu, Ala, CML or Ile; Xaa_c is either Lys or Orn, the side chain of which may be linked in an amide cyclizing bond to that of Glu; and C is a sequence of the last 7 amino acid residues of the C-terminal portion of any peptide of the CRF family; provided that Nle or Leu may be substituted for Met in A, B and/or in C.